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| APPLICATION NO.   | FILING DATE                           | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.     | CONFIRMATION NO |
|---|---------------------------------------|----------------------|-------------------------|-----------------|
| 09/996,263  | 11/28/2001                            | Phillip Dan Cook     | ISIS-4943               | 3783            |
| 32650 7   | 7590 10/31/2003                       |                      | EXAMINER                |                 |
| WOODCOCK WASHBURN LLP<br>ONE LIBERTY PLACE - 46TH FLOOR |                                       |                      | SCHULTZ, JAMES          |                 |
|   | Y PLACE - 461H FLOOI<br>IIA, PA 19103 | (                    | ART UNIT PAPER NUMBER   |                 |
|   | •                                     |                      | 1635                    |                 |
|   |                                       |                      | DATE MAILED: 10/31/2003 | 3               |

Please find below and/or attached an Office communication concerning this application or proceeding.

|   | Application No.                 | Applicant(s)               |   |  |  |  |  |
|---|---------------------------------|----------------------------|---|--|--|--|--|
| Advisory Action   | 09/996, 263                     | COOK ET AL.                |   |  |  |  |  |
| Advisory Action   | Examiner                        | Art Unit                   |   |  |  |  |  |
|   | J. Douglas Schultz              | 1635                       |   |  |  |  |  |
| The MAILING DATE of this communication app ars on the cover she t with the correspond nc address  |                                 |                            |   |  |  |  |  |
| THE REPLY FILED 14 October 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may <u>only</u> be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.  |                                 |                            |   |  |  |  |  |
| PERIOD FOR REPLY [check either a) or b)]  |                                 |                            |   |  |  |  |  |
| a) The period for reply expires 3 months from the mailing date of the final rejection. b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).  Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). |                                 |                            |   |  |  |  |  |
| 1. A Notice of Appeal was filed on Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.  |                                 |                            |   |  |  |  |  |
| 2. The proposed amendment(s) will not be entered because:   |                                 |                            |   |  |  |  |  |
| (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);  |                                 |                            |   |  |  |  |  |
| (b) ☐ they raise the issue of new matter (see Note below);  |                                 |                            |   |  |  |  |  |
| (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  |                                 |                            |   |  |  |  |  |
| (d) they present additional claims without canceling a corresponding number of finally rejected claims.   |                                 |                            |   |  |  |  |  |
| NOTE:   |                                 |                            |   |  |  |  |  |
| 3. Applicant's reply has overcome the following rejection(s):   |                                 |                            |   |  |  |  |  |
| 4. Newly proposed or amended claim(s) would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).   |                                 |                            |   |  |  |  |  |
| 5.⊠ The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.  |                                 |                            |   |  |  |  |  |
| 6. The affidavit or exhibit will NOT be considered becaused by the Examiner in the final rejection.   | cause it is not directed SOLELY | to issues which were newly | 1 |  |  |  |  |
| 7. For purposes of Appeal, the proposed amendment explanation of how the new or amended claims we   |                                 |                            |   |  |  |  |  |
| The status of the claim(s) is (or will be) as follows:  |                                 |                            |   |  |  |  |  |
| Claim(s) allowed:   |                                 |                            |   |  |  |  |  |
| Claim(s) objected to:   |                                 |                            |   |  |  |  |  |
| Claim(s) rejected: 8-13 for reasons of record.  |                                 |                            |   |  |  |  |  |
| Claim(s) withdrawn from consideration:  |                                 |                            |   |  |  |  |  |
| 8. The proposed drawing correction filed on is a) approved or b) disapproved by the Examiner.   |                                 |                            |   |  |  |  |  |
| 9. Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s)   |                                 |                            |   |  |  |  |  |
| 10. Other:  |                                 |                            |   |  |  |  |  |
|   |                                 |                            |   |  |  |  |  |

Continuation of 5. does NOT place the application in condition for allowance because: applicants' reply and declaration pertaining to the parent specifications' support for the broad scope of any oligo containing more than one different modification is not considered convincing. The arguments contained therein have been addressed in full in the final Office action. Briefly, applicants argue that the specifications of the parent documents in question (which both disclose similar subject matter) exemplify one oligo containing both 2'-methyl and 2'-methylthio modifications, and furthermore disclose a broad list of modifications. Applicants argue that one of skill the specification would lead one of skill to combine these teachings to make a broad scope of oligos, wherein said oligos must contain at least two different modifications chosen from said broad list.

However, in response it is pointed out that applicants have not pointed out with any specificity where such a nexus exists. To reiterate, applicants are considered to have the scope of support pertaining to oligos containing 2'-methyl and 2'-methylthio modifications. However, this one oligo is not considered to provide support for any oligo containing any two different modifications from said broad list. Furthermore, the examiner has not been able to locate any teaching beyond the one exemplified oligo that would lead one to combine the teachings as claimed by applicants to make any other oligo that must contain at least two different modifications chosen from said broad list. Even where the specification does teach the one exemplified oligo, there is no mention that this one combination is desireable or useful in any way, let alone that other combinations may be desireable or useful. Applicants also suggest that the mere listing of numerous modifications somehow stands as proof that they were contemplated as being used in combination on the same oligo. In fact, the lists of modifications pointed to by applicants to support their arguments appear directed only to oligos containing one type of modification, because the list specifically recites the alternative language "or", which would lead one of skill to interpret that the modifications were not contemplated as useful together. Here too, applicants have pointed to no mention or suggestion that two or more modifications on the same oligo were ever contemplated. In summary, although applicants have pointed to one exemplifed oligo containing 2'-methyl and 2'-methylthio modifications, this does not provide specific written support for oligos that must be comprised of more than one such modifications selected from the broad list of halo, azido, amino, alkoxy, thioalkoxy, alkylamino, and alkyl modifications because beyond the exemplifed oligo, applicants have not indicated where such oligos containing more than one different 2'-modifications are referenced or even suggested.

> SEAN MCGARRY PRIMARY EXAMINER